At page 11, after the first paragraph, please insert the following paragraph:

Figure 10. Viruses were incubated with serial 5-fold dilutions of antibody (plasma) and used to infect U-87/CD4/CCR5/CXCR4 target cells. Serial virus samples (columns) were tested against serial antibody samples (rows) using a matrix format. Neutralization values represent the plasma (antibody) dilution required to inhibit virus infectivity by 50% (IC50). The larger the number, the larger the dilution, reflecting higher antibody neutralization titers. Sample collection dates are represented as mm/dd/yy. The neutralizing activity of each plasma sample was also tested against two reference viruses: NL4-3 (X4 laboratory strain), JRCSF (R5 primary isolate).

At page 59, please delete the paragraph that begins "In one embodiment ..." and replace it with the following paragraph:

In one embodiment, drug resistance mutations were introduced into well-characterized X4 tropic (NL4-3) and R5 tropic (JRCSF) viruses. T20 susceptibility was measured using the virus entry assay (**Figure 7**). The fold change (FC) in T-20 susceptibility for each virus was determined by dividing the IC50 of the test virus by the IC50 of the HXB2 strain of HIV-1. T-20 sensitivity of similar mutant viruses bas been reported in the scientific literature (Rimsky, et al.). In this embodiment, viruses with one mutation within the GIV motif of gp41 (DIV, GIM, SIV) were less susceptible to T20 than the wildtype virus (GIV). Viruses with two mutations within the GIV motif (DIM, SIM, DTV) were less susceptible to T20 than with one, or no mutations in the GIV motif.

At page 59-60, please delete the paragraph that begins "In another embodiment ..." and replace it with the following paragraph:

In another embodiment, mutations that may confer reduced (or increased) susceptibility to the entry inhibitor are identified by sequencing the envelope genes of the sensitive and resistant viruses. The deduced amino acid sequences of the sensitive and resistant viruses are compared to identify candidate drug resistance mutations. The ability of a specific mutation to confer altered drug susceptibility is confirmed or disproved by introducing the mutation into a drug sensitive virus and measuring the susceptibility of the mutant virus in the virus entry assay. In the example represented here, a short stretch of amino acid sequences within

antibody preparation (typically for 1 h) that is being evaluated. The sera or antibody preparations are tested undiluted and at incrementally greater dilutions (typically four to five serial 5- or 10-fold dilutions). Infection of target cells with each virus stock also is performed in the absence of antibody (no antibody). Virus neutralization is assessed by comparing the amount of luciferase activity produced in target cells, both in the presence and absence of antibody. In this embodiment, the results of the assay are determined by comparing the ability of antibodies derived from the patient at different time points to preferentially block infection of target cells (reduce or eliminate luciferase activity) of the pseudotyped viruses derived from the patient at different time points. Virus neutralization activity is quantified by noting the highest antibody dilution (most dilute) that is able to block target cell infection (*e.g.*, the highest dilution that is able to reduce the luciferase activity produced in the absence of antibody by 50%). Thus, this embodiment allows one to assay in a patient the co-evolution over time of immunologically distinct HIV strains and the neutralizing antibody response.

This method was used on a group of 14 treatment-naive patients with primary HIV infection. Plasma specimens were drawn from each patient at 2-4 month intervals (average follow up was 18 months, with a range of 6-39 months). Viruses were incubated with serial 5-fold dilutions of antibody and used to infect target cells that expressed CD4 plus the CCR5 and CXCR4 co-receptors. It was found that 12 of the 14 patients generated strong neutralizing antibody responses to virus. Data from a representative patient are provided in Figure 10. However, each sequential virus consistently and rapidly escaped the concurrent neutralizing antibody response. Peak neutralization titers (average 1:1497 dilution, range 1:339-1:4627) developed several months after a virus emerged and the response remained elevated for many months, to years, thereafter. Neutralizing antibody titers were generally greater to early viruses than to later viruses from the same patient. Neutralization responses to a heterologous R5 primary virus (JR-CSF) were weak and delayed. Responses to a X4 lab strain (NL4-3) increased over time, but varied in intensity among patients. The magnitude of neutralizing antibody response to autologous virus did not correlate with mean plasma HIV RNA or duration of HIV infection. Thus, the rate of viral neutralization escape is remarkable and indicates that neutralizing antibody can exert a previously unappreciated level of selective

the first heptad repeat (HR-1) of the HIV-1 gp41 transmembrane envelope protein is aligned for viruses exhibiting different T-20 susceptibilities. Highlighted amino acids represent mutations known to confer reduced susceptibility to T-20.

At page 77, before the paragraph titled "EXAMPLE 7", please insert the following paragraphs:

Characterization of Patient HIV-1 (patient virus v. patient antibody)

This example provides a method for detecting within a patient the evolution of a neutralizing antibody response and of viral strains that evade the neutralizing response. In this embodiment, the assay is performed using a target cell line that expresses the HIV-1 receptor CD4 plus the HIV-1 co-receptors CCR5 and CXCR4 (U87/CD4/CCR5/CXCR4 or HT4/CCR5/CXCR4). Such a cell line is capable of evaluating the neutralizing activity of antibodies for both R5 and X4 tropic viruses. In a related embodiment, the assay is performed using two target cell lines. One cell line expresses CD4 plus CCR5 (U-87/CD4/CCR5) and is used to test R5 tropic viruses. Another cell line expresses CD4 plus CXCR4 (U-87/CD4/CXCR4) and is used to evaluate X4 tropic viruses. The virus entry assay is performed by infecting individual target cell cultures with recombinant virus stocks derived from packaging host cells transfected with pHIVenv and pHIVΔ or pHIVΔ DU3 vectors. In this embodiment, pHIVenv vectors contain patient virus derived envelope sequences and express HIV-1 envelope proteins (gp120SU, gp41TM). In this embodiment, different virus populations are used to construct pHIVenv vectors. The different virus populations are derived from serial (*i.e.*, longitudinal) plasma specimens (*i.e.*, viruses collected from the same patient at different time points). Pseudotyped HIV derived from pHIVenv vectors are evaluated in the virus entry assay to determine if they are susceptible to neutralization by a panel of antibodies that are derived from serial plasma specimens from the patient. Thus, in this embodiment, the same patient is the source of both the virus populations and the antibodies. In this embodiment, viruses are evaluated using target cells cultured in, for example, 96 well plates. Typically, target cells are plated at 10,0000 cells per well for the U-87/CD4/CCR5/CXCR4, U-87/CD4/CCR5 and U-87/CD4/CXCR4 cell lines or at 5,000 cells per well for the HT4/CCR5/CXCR4 cell line. Target cells are plated on the day of infection. Prior to target cell infection, each virus stock is pre-incubated with the sera or